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Environmental Tobacco Smoke
and Its Relationship to Lung Cancer

Public debate recently has focused on the effects of smoking on nonsmokers. Those who argue for widespread bans on smoking sometimes claim that nonsmokers can suffer lung cancer as the result of exposure to environmental tobacco smoke ("ETS"), which is the smoke that enters the air either from the end of the burning cigarette or when exhaled by smokers. Scientific research, however, has failed to support this claim. To the contrary, as the American Cancer Society recently recognized, "the currently available evidence is not sufficient to conclude that passive or involuntary smoking causes lung cancer in nonsmokers * * * *"[1]

The Cancer Society reached its conclusion despite the fact that some studies have suggested that exposure to ETS can increase a nonsmoker's risk of contracting lung cancer by 35 to 40 percent.[2] Implicit in the Cancer Study's conclusion is the recognition that there exist strong reasons to doubt the validity of these estimates. Among other things, the pertinent studies frequently have ignored fundamental maxims of scientific research, reaching conclusions without taking account of all the factors that may contribute to the development of a disease such as lung cancer. As this paper discusses below, when all the relevant factors are taken into account, the only fair

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conclusion is that the supposed link between ETS and lung cancer remains unproven.

How Much Exposure to Tobacco Smoke?

Two basic issues must be considered when evaluating the potential risks of ETS. The first has to do with how much exposure nonsmokers really have to ETS. The second concerns the statistical studies that have been performed to determine whether certain groups of nonsmokers have higher rates of lung cancer simply because they have lived or worked with nonsmokers.

The first issue involves efforts to estimate the amount of tobacco smoke to which a typical nonsmoker is exposed, compared to the amount that is inhaled by active smokers. Scientists have conducted several such studies, which show that the exposure of nonsmokers to ETS is minimal. For example, on average a nonsmoker is exposed to no more than one-quarter of one percent of the smoke inhaled by an active smoker.[3] In terms of the particulate matter retained by nonsmokers, the amount is even lower: recent studies have estimated that the average nonsmoker retains only one-fifth of one percent of the particulate matter retained by active smokers.[4]

Faced with these facts, smoking opponents have responded with the assertion that ETS is somehow more toxic than the smoke inhaled directly by smokers. They claim that the smoke from the burning end of a cigarette -- called sidestream smoke -- contains higher amounts of some potentially harmful constituents than the mainstream

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smoke inhaled by smokers. To support this assertion, they have pointed to laboratory tests using smoking machines and enclosed chambers, with smoke constituents being measured at a distance of only a few centimeters from the end of a burning cigarette.

A central problem with this type of experiment is the artificial and unrealistic conditions under which it is conducted. In normal life, sidestream smoke is not collected in small chambers; instead, it initially exists only in small amounts and then is immediately diluted in the surrounding air. Scientists estimate that under such normal conditions, ETS constituents such as nicotine exist in amounts equal to less than 1/100th of those found in mainstream smoke.[5]

Based on the low levels of sidestream smoke encountered by the typical nonsmoker, it appears unlikely that exposure to ETS could cause a substantially increased risk of lung cancer. Indeed, based on these dosage levels, if one assumes that active smoking increases the relative risk of lung cancer ten-fold (a common assertion), then, based on the amount of sidestream smoke typically inhaled by a nonsmoker, ETS could at most increase the risk of lung cancer by only one five-hundredth of a percent. This level of increased risk, if it exists at all, is so small that it would defy biological or epidemiologic confirmation.

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Epidemiological Studies: The Problems in Research

In addition to assessing exposure levels, scientists have sought to estimate the effects of ETS by conducting epidemiological studies. Such studies attempt to identify two population groups, one having been exposed to ETS and the other reporting no exposure. Scientists then estimate and compare the lung cancer rates experienced by each group. Such studies have yielded conflicting results, with two early studies finding that there was a correlation between exposure to ETS and lung cancer, and most later studies concluding that no statistically-significant relationship exists. In trying to make sense of these studies, two important factors should be noted.

The Problem of Misdiagnosis. First, there exist several types of lung cancer. Some of these have been linked to smoking, while others bear no relationship at all. For example, there is an important distinction between primary lung cancer and secondary lung cancer. Primary lung cancer, which sometimes has been linked to smoking, begins and develops in the lung. Secondary lung cancer is cancer that begins elsewhere in the body but spreads to the lung in the same way that cancer anywhere in the body sometimes spreads to other parts of the body.[6]

In assessing whether there is a relationship between ETS and lung cancer, the distinction between primary and secondary cancer is paramount. Secondary lung cancer results from other cancers and plainly bears no relation-

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ship to smoking. Thus, if a scientific study fails to distinguish between primary and secondary lung cancers, it may falsely overestimate the number of cancer incidents possibly linked to smoking.

In practical application, this problem recurs in two common situations. First, some studies have relied only on hospital records or death certificates that have listed a patient as having had lung cancer, without identifying whether the patient had primary or secondary lung cancer. Such a determination requires a skilled review of slides of the cancer cells themselves. Without this expertise and analysis, it is very difficult to determine the precise type of cancer involved.[7]

Second, the problem of misdiagnosis is particularly important when analyzing the possible effects of ETS on women. Women sometimes are afflicted with breast or ovarian cancer that spreads to the lung. Unless a careful effort is made to identify the original source, epidemiological studies will not accurately identify the type of cancer involved.[8] This problem is particularly important in this context because many studies on ETS have evaluated the effects of ETS on nonsmoking women married to smokers.

The Failure To Isolate All Variables. A second broad problem in ETS studies is the failure to ensure that observed effects may be explained only by ETS. In all research on ETS, a scientist must control carefully for all other variables in order to focus on ETS and not some other factor. Most epidemiological studies have focused

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on individual nonsmokers who have been married to smokers. Without accounting for other variables, however, this is not likely to lead to reliable results. For example, lung cancer -- like all cancers -- tends most often to afflict those of an advanced age. Thus, when comparing two population groups, one must compare groups with closely similar age distributions.

In addition, studies must be careful to isolate ETS from other variables that may cause lung cancer, such as poor diet and fitness, and occupations that expose workers to indoor and outdoor air pollution. This is particularly important because individuals who smoke are not randomly distributed in society. In some countries, families with smokers tend to fall disproportionately in lower income classes, where diet is often not as healthy and there is a greater chance of employment in an occupation with exposure to air pollution. If a study fails to control for these factors, it may conclude falsely that ETS is contributing to cancer when in fact the determinative factor may be something entirely different.

Epidemiological Studies: The Results

Not surprisingly, the results of epidemiological studies have closely reflected the extent to which they have successfully avoided problems of misdiagnosis of symptoms and mischaracterization of other variables. The debate in the scientific community began in earnest in 1981 with studies conducted in Japan (the Hirayama study) and Greece (the Trichopoulos study).[9] These studies con-

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cluded that women who were married to smokers had a greater chance of developing lung cancer than women married to nonsmokers.

Numerous subsequent studies have criticized the methodologies of these two reports. For example, a participant in a 1987 Tokyo conference published a report that questioned the Hirayama study's statistical methodology and criticized the study's failure to report or evaluate "dietary and occupational factors known to influence susceptibility to lung cancer."[10] In 1988, two reports for a conference in the United Kingdom stated that the Hirayama study had failed to divide the study population into appropriate age groups. The reports found that when such age bias was removed, the purported risk to nonsmoking wives disappeared completely.[11]

Similarly, many scientists have criticized the Trichopoulos study for numerous flaws, including the failure to diagnose carefully the nature of the lung cancers involved. The authors of the Trichopoulos study themselves noted in 1983 that their research had been "criticized (by ourselves and others) because of the small number of subjects, because several tumors lacked histological confirmation, and because controls and cases were from different hospitals."[12]

Research into the health effects of ETS continues, and some of the more recent studies have made important advances in improving upon the methodologies utilized in the Hirayama and Trichopolous studies. These include two recent studies that, for the first time, have incorpo-

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rated microscopic work by pathologists to identify the types of cancers involved. Dr. Linda C. Koo at the University of Hong Kong has headed a series of research efforts that have combined the work of a pathologist to identify cancers with strict controls to separate the effects of other variables such as age and diet.[13] In the words of one independent reviewer, "the information on the patients and controls [in the Koo studies] is more detailed than in all other studies."[14]

The research by Dr. Koo and her colleagues led to several conclusions. Most important, it determined that when problems of misdiagnosis and independent variables were removed, ETS exposure in the home and at work had no statistically significant impact on the incidences of lung cancer.

The Hong Kong study also dramatically underscored the significance of the failure of many other studies to isolate variables associated with socio-economic status. The research showed that the wives of smokers were typically less wealthy and had less "healthy" lifestyles, including diets consisting of more processed foods and fewer fresh fruits and vegetables. Dr. Koo concluded that these correlates -- when not isolated -- played an important role in confounding research results.[15]

Researchers with the American Cancer Society in New York have conducted similarly thorough cancer identification research. A team of researchers headed by Dr. Lawrence Garfinkel worked with a pathologist who reviewed

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for each patient a series of medical slides of actual cancer cells. This review showed that overall there was no statistically significant increase in the risk of lung cancer for nonsmoking women married to smokers. Indeed, ETS caused even a marginally significant risk increase for only one subgroup -- women married to men who smoke more than 20 cigarettes per day.[16]

These two studies cast substantial doubt on the validity of the 1981 research that sparked the ongoing debate on the effects of ETS. In a 1987 article, a German scientist reviewed all of the research conducted since 1981 and concluded that "the major trend of the evidence" does not support the hypothesis that exposure to ETS causes lung cancer.[17] Indeed, the article noted that "all studies with positive associations [between ETS and lung cancer] can just as well be explained by chance, bias, confounding or misclassification."[18]

Conclusions

At present, it is simply not fair to conclude that exposure to ETS increases the risk of lung cancer among nonsmokers. Advocates of such a conclusion typically rely on incomplete or inadequate research, while ignoring both the immediate dilution of sidestream smoke and the more recent (and more thorough) scientific studies that have found no statistically significant relationship between ETS and lung cancer.

Scientific research on ETS should continue. There is still room for improvement in research tech-

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niques, even in some of the most thorough studies such as the Garfinkel work. Critically, however, if this research is to be meaningful, it must proceed in a manner that carefully and properly accounts for such problems as misdiagnosis and the effects of factors such as age, diet and occupational exposure to air pollution. In the meantime, the only fair conclusion is that ETS has not been shown to increase the nonsmoker's risk of lung cancer.

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